Late Positive Component Amplitude in Schizophrenics and Alcoholics in Two Different Paradigms

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Abstinent alcoholics, unmedicated schizophrenics, and controls were tested in two paradigms designed to elicit the late positive component. Experiment A used frequent stimuli of differing incentive value and Experiment B used infrequent stimuli of differing perceptual discriminability. Alcoholics and schizophrenics showed late positive components that were significantly reduced in amplitude compared to controls. The patient groups were similar in their late component amplitudes. Control subjects showed a substantially wider response range than the patient groups. The narrow response range in both patient groups was manifested in diminished late component amplitudes to both stimuli in both experiments. The intraclass correlation coefficient of late component amplitudes for both patient groups was significantly greater than that of the controls.

Introduction

The late positive complex of the event-related potential (ERP) has been studied in a wide variety of experimental contexts, including the oddball paradigm (Duncan-Johnson and Donchin 1977), stimulus incentive paradigm (Johnston and Holcomb 1980; Begleiter et al. 1983), and a variety of target detection tasks (Squires et al. 1977). It is not well established whether or not the late component recorded in these experiments is a single wave or a family of waves (Roth 1978; Friedman et al. 1981).

Substantial reductions of late positive component (LPC) amplitude have been described in schizophrenic (Roth et al. 1980; Brecher and Begleiter 1983), alcoholic (Pfefferbaum et al. 1979; Porjesz and Begleiter 1981, 1985), demented (Goodin et al. 1978), and depressed (Pfefferbaum et al. 1984) patients. Studies of clinical populations have utilized a variety of different paradigms to elicit the LPC, but each study has generally employed one paradigm. This pattern of investigation does not exclude the possibility that a patient group that had an abnormal response in one paradigm might have a normal LPC in a different paradigm. A consistent diminution of LPC amplitude in two or more paradigms would suggest a generalized deficit. Testing patient populations in several paradigms also

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raises the possibility of distinguishing between them on the basis of a different pattern of response.

We analyzed data from two very different paradigms in control subjects, schizophrenics, and abstinent alcoholics. Experiment A required responses to equiprobable stimuli that had differential incentive value, and Experiment B required responses to infrequent targets of differing perceptual discriminability. We were interested in estimating the consistency of the LPC across the two paradigms. If the LPC was similar in the two experiments, it would suggest that the same wave was elicited in both cases. If the subjects' responses in Experiment A were not correlated with their responses in Experiment B, it would imply that different LPCs were elicited in each case. Another interpretation could be that there is only one LPC that has a broad dynamic range and is influenced by the experimental context and the internal state of the subject. This analysis would also indicate whether or not alcoholic and schizophrenic patients show consistently reduced LPCs and whether or not the two patient groups are distinguishable on the basis of their LPC response.

Methods

Subjects

The subjects were part of a larger group of individuals who had been tested in both paradigms. The schizophrenic patients were diagnosed by two psychiatrists using DSM-III criteria. These patients had not been taking any psychoactive medication for at least 2 weeks, with the exception that some patients were allowed one dose of a hypnotic medication at bedtime up to 3 days prior to testing. They had a mean age of 28.9 years ($\pm$8.9); there were 6 men and 4 women.

The alcoholic patients, 8 men and 3 women, were inpatients on an alcohol detoxification ward; they were right-handed, were diagnosed by Research Diagnostic Criteria (RDC), and had a mean age of 35.7 ($\pm$7.5) years. They had been drinking for an average of 13.4 years, had been abstinent from alcohol for an average of 3.85 weeks, and had been free of alcohol and any psychoactive medication for a minimum of 3 weeks. These patients did not have clinical signs of central nervous system (CNS) disease or liver disease and did not have histories of other drug abuse, head trauma, or seizures unrelated to withdrawal from alcohol.

The control subjects were solicited by advertisement and were screened for psychiatric illness and substance abuse. Eleven men and 2 women, mean age 26.6 years ($\pm$4.6), were tested. The three subject populations were unmatched with respect to socioeconomic status, education, and intelligence.

Procedure

Experiment A was presented first and consisted of three runs. In each run, the stimuli 0.00 and 1.00 were presented 30 times in random sequence. The stimuli were displayed at the center of a CRT screen, were equal in size and intensity, subtended 2.7° of arc, were of 15 msec duration, and were presented at randomly varying interstimulus intervals of 2–5 sec. In the first run, the subjects were told to press one of two buttons after each stimulus. Prior to the second run, the subjects were told that they would receive a dollar

for every correct press following a 1.00 stimulus, would receive no reward for a correct press following a 0.00 stimulus, and would be penalized a dollar for every stimulus not followed by a correct press. Instructions for run 3 were the same as run 2, except that the subjects were told to press as quickly as possible and that failure to respond within criterion time (350 msec) would result in a dollar penalty. Thus, both stimuli had incentive value in runs 2 and 3, with the 1.00 stimulus having greater incentive value than the 0.00 and run 3 being more demanding than run 2.

Experiment B always followed the incentive experiment. This paradigm consisted of 180 presentations of a vertical line (nontarget), 30 presentations of a horizontal line (easy target), and 30 presentations of a line that deviated from the vertical by 3 degrees (difficult target). The 240 stimuli were presented in random sequence, with the identical stimulus parameters as in the incentive experiment, except for the duration of the stimulus, which was 5 msec in this case. The subjects were instructed to press a button as quickly as possible after every target. Complete protocols have been published elsewhere (Begleiter et al. 1983; Porjesz et al. 1987).

Data Collections and Analysis

Evoked potentials were recorded at the scalp with gold cup electrodes placed at midline frontal (Fz), central (Cz), parietal (Pz), occipital (Oz), left parietal (P3), and right parietal (P4) locations according to the 10-20 International System. Linked ears were used as reference. Only the midline parietal data are presented here. Time-locked averages of electrical activity at Pz were computed for those trials that did not contain excessive ($\geq$20 μV) eye movement artifact and to which a correct response was made. The present analysis included only those subjects who had at least 15 correct responses free of eye movement artifact ($\geq$20 μV) to each target in both experiments. All subjects but one schizophrenic had at least 20 such responses. Ten schizophrenic patients met the above criteria, 9 of whom were inpatients. Averages were computed for the 1.00 stimulus in runs 2 and 3 of Experiment A and to the 3° and 90° targets in Experiment B. The late positive component was identified independently by two raters not blind to diagnosis. Baseline electrical activity, defined as the average voltage during the 49-msec preceding stimulus onset, was subtracted from the peak amplitude.

Analysis of variance with three groups and four repeated measures was performed on the baseline to peak voltages recorded at the parietal electrode with correction for repeated measures (Geisser and Greenhouse 1959). The correlation matrix of the four voltages was computed for each of the three groups. *z* Scores were computed for each schizophrenic and alcoholic patient. The intraclass correlation coefficient was calculated for the individual values for the three groups and for the *z* scores for the patient groups. The intraclass coefficients were transformed and compared by Fisher's method (Cohen and Cohen 1975).

Results

Alcoholic and schizophrenic patients had significantly reduced late component amplitudes compared to controls ($F = 7.67$, $p < 0.02$) (Figure 1). Individual two-tailed *t*-tests showed the schizophrenic group to have lower amplitudes compared to controls for all four measures (Table 1). Late component amplitude was also reduced in alcoholics relative

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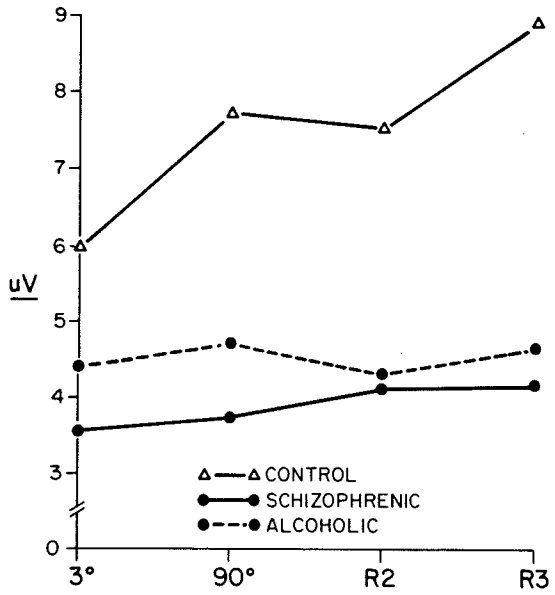

Figure 1. Mean late component amplitudes at Pz to each of four target stimuli for schizophrenics, alcoholics, and controls.

to controls on three of the four measures (Table 1). The exception was the 3° target, where the difference approached significance ($p < 0.1$). None of the differences between the schizophrenic and alcoholic groups was significant (Table 1).

Within-group *t*-tests were done for each group on the run 2 − run 3 difference and the 3° − 90° difference. In Experiment A, the controls' increased response to the 1.00 stimulus in run 3, compared to their response to this stimulus in run 2, approached significance ($t = 2.00$, $p < 0.1$). In Experiment B, the controls' response to the easy target was larger than the response to the difficult target ($t = 3.14$, $p < 0.01$). There was no difference in either patient group on either within-paradigm comparison. Differences between stimuli and stimuli–group interactions were not significant.

For all groups, the within-paradigm (3°–90° and run 2–run 3) late component amplitudes were significantly correlated (Table 2). For the controls, none of the cross-paradigm correlations were significant. For alcoholic patients, the late component in run 2 was

Table 1. Pained Comparisons

	Schizophrenic–control			Alcoholic–control			Schizophrenic–alcoholic		
3°									
Mean (μV)	3.47		5.85	4.30		5.85	3.47		4.30
p		<0.05			<0.1			NS	
90°									
Mean	3.69		7.52	4.60		7.52	3.69		4.60
p		<0.01			<0.02			NS	
Run 2									
Mean	4.06		7.35	4.25		7.35	4.06		4.25
p		<0.05			<0.02			NS	
Run 3									
Mean	4.11		8.71	4.55		8.71	4.11		4.55
p		<0.01			<0.01			NS	

Table 2. Correlation Matrix

	Within paradigm		Across paradigm			
	3°–90°	R2–R3	R2–3°	R2–90°	R3–3°	R3–90°
Control						
r	0.64	0.74	0.54	0.35	0.21	0.06
p	<0.02	<0.01	NS	NS	NS	NS
Alcoholic						
r	0.80	0.85	0.69	0.76	0.46	0.60
p	<0.01	<0.01	<0.02	<0.01	NS	NS
Schizophrenic						
r	0.76	0.68	0.49	0.53	0.70	0.80
p	<0.02	<0.05	NS	NS	<0.05	<0.01

significantly correlated with the amplitude to both targets in Experiment B. For the schizophrenics, late component amplitude in run 3 was correlated with the amplitude recorded to both targets in Experiment B.

Intraclass correlations are presented in Table 3. For the controls, this correlation was not significant, whereas for the patients, the result was highly significant (for schizophrenics, $r = 0.963$, $p < 0.01$; for alcoholics, $r = 0.977$, $p < 0.01$). *t*-Test comparisons of z' transformed intraclass correlation coefficients showed that both groups differed significantly from the control group ($p < 0.02$ for schizophrenics; $p < 0.01$ for alcoholics). The patient groups did not differ from each other. Intraclass correlations of individual *z*-transformed scores were also significant for schizophrenics ($r = 0.849$, $p < 0.05$) and for alcoholics ($r = 0.778$, $p < 0.05$). The between-group difference was not significant.

Seventy-six of the patients' 84 *z*-scores (4 measures, 21 patients) were within 2 standard deviations of the control mean. Eight patients (6 schizophrenics and 2 alcoholics) had *z*-scores greater than 2 on at least 1 of the 4 measures. With the exception of one schizophrenic patient, all of these patients' LPC amplitudes were at least 1 SD below the control mean on all 4 measures.

Reaction times are presented in Table 4. There was no significant effect of diagnosis (${}_2F_{31} = 1.72$; $p > 0.15$) or diagnosis × stimulus interaction (${}_6F_{93} = 1.16$; $p > 0.3$).

Table 3. Intraclass Correlations

	Intraclass correlation—Amplitudes			
	r	*f*	*p*	Z'^a
Controls	0.428	3.99	NS	0.458
Alcoholics	0.977	174.9	<0.01	2.230
Schizophrenics	0.963	105.9	<0.01	1.987
		Intraclass correlation—*z* Scores		
Alcoholics	0.778	15.05		<0.05
Schizophrenics	0.849	23.61		<0.05

[a]Transformed correlation coefficient (as distinguished from *z* score).

Table 4. Reaction Times (msec)

	3°	90°	Run 2	Run 3
Schizophrenics	674.8	644.4	776.2	608.7
	(196.6)[a]	(198.5)	(339.1)	(198.3)
Alcoholics	587.3	528.2	683.9	510.0
	(118.6)	(91.4)	(181.6)	(137.5)
Controls	607.2	533.4	682.4	425.8
	(141.0)	(95.7)	(183.6)	(102.2)

[a]SD.

There was a significant within-subject effect ($_3F_{93} = 29.54$; $p < 0.001$, corrected for repeated measures) reflecting the different levels of task difficulty across and within paradigms.

The mean number of artifact-free correct responses for each group are listed in Table 5. There were significant group ($_2F_{31} = 10.69$; $p < 0.001$), stimulus ($_3F_{93} = 22.07$; $p < 0.001$, corrected for repeated measures), and group × stimulus ($_6F_{93} = 8.27$; $p < 0.001$, corrected for repeated measures) effects. Post hoc *t*-tests revealed that the controls had more correct responses than the schizophrenics to the 3° target ($p < 0.005$) and to the 90° target ($p < 0.001$). The alcoholic patients also had more correct responses than the schizophrenic patients to the 3° target ($p < 0.001$) and to the 90° target ($p < 0.001$).

Discussion

The consistent reduction of LPC amplitude in schizophrenics and alcoholics in both experiments suggests that this deficit is independent of the task used to elicit the LPC and that this deficit represents a physiological abnormality in these patients. The reduction in amplitude in both paradigms demonstrates an abnormality over a range of task demands. The late positive component is reduced in schizophrenics and alcoholics regardless of whether the stimuli are equiprobable or infrequent, easy or difficult to detect, or associated with a reward. These stimulus characteristics cover much of the gamut of stimuli used to study these populations, and it is reasonable to speculate that the late positive component is reduced in schizophrenics and alcoholics in all visual attention-dependent paradigms.

A second feature of the late positive component in schizophrenics and alcoholics is the static nature of their response, as can be seen in the within paradigm results. Control subjects have shown significantly larger late component amplitudes to the 1.00 stimulus in run 3 compared to run 2 (Begleiter et al. 1983) and larger late component amplitudes to the 90° target than to the 3° target (Porjesz et al. 1987). These effects are clear in

Table 5. Correct Responses

	3°	90°	Run 2	Run 3
Schizophrenics	21.70	22.40	28.40	28.60
	(3.95)[a]	(3.86)	(2.07)	(1.78)
Alcoholics	28.18	28.72	28.36	29.18
	(3.00)	(1.85)	(2.16)	(0.98)
Controls	26.69	28.15	28.85	29.54
	(3.12)	(2.44)	(3.05)	(0.67)

[a]SD.

Figure 1, but are less compelling statistically, possibly because of the smaller ($n = 13$) sample size. Both patient groups had the same response to each stimulus in each experiment.

The consistent reduction of the late positive component in schizophrenic patients reported here and unanimously in the literature suggests that this abnormality may be a feature of the "defect state" of Type 2 schizophrenia (Crow 1980). A failure to respond electrophysiologically to high-incentive stimuli has been reported in anhedonic college students (Simons 1982). Anhedonia, a common feature of defect state schizophrenia, has also been observed in abstinent alcoholics (Martin et al. 1978). The relationships between the late positive component and deficit symptoms are under study in our laboratory.

Reductions of LPC amplitude could have applicability to assessment and diagnosis. However, Pfefferbaum et al. (1984), using an oddball paradigm, were unable to distinguish among schizophrenic patients, depressed patients, and patients with Alzheimer's disease. The lack of significant differences in LPC amplitude between our schizophrenic and alcoholic patients may reflect neuropathology of different etiology but at the same brain loci in both populations. Possible generators for the LPC have been reported in the medial temporal region, specifically in the hippocampus, hippocampal gyrus, and amygdala (Halgren et al. 1980) and in the frontal lobe (Mccarthy 1985). Schizophrenics have been shown to have decreased hippocampal size (Bogerts et al. 1985), decreased cortical thickness of the parahippocampal gyrus (Brown et al. 1986), increased size of the temporal horn of the lateral ventrical (Brown et al. 1986), disorganized pyramidal cell architecture within the hippocampus (Kovelman and Scheibel 1984), decreased frontal blood flow (Ingvar and Franzen 1974), and decreased frontal cerebral glucose uptake (Buchsbaum et al. 1984). Neuronal loss has been reported in the hippocampi of rats who chronically consumed ethanol (Walker et al. 1980). Computed tomography scan (Cala and Mastaglia 1981) and autopsy studies (Courville 1955) have revealed frontal lobe damage in alcoholics.

The wide range of late component amplitudes observed in normal subjects can be interpreted as evidence that the two tasks may elicit different late positive components. The data are also consistent with the view that in normal subjects, the amplitude of the LPC has a broad dynamic range dependent on the internal state of the subject and the specific characteristics of the stimulus and task. In either case, this dynamic range is severely constricted or possibly absent in schizophrenics and alcoholics.

The small sample sizes and the restricted number of target stimuli in each paradigm suggest caution in interpreting these results. The data demonstrate a dynamic range of LPC responsiveness in normal subjects and a reduced static response in alcoholics and schizophrenics. These responses reliably distinguish patients from controls, but not from each other. Differential diagnosis by electrophysiological means (Begleiter and Porjesz 1986) will require measurement of several evoked potential components in addition to the late component of the ERP.

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